UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/846,758	05/01/2001	Alex Liu	EP01-001C	4859

23500 7590 07/30/2003

JAN P. BRUNELLE
EXELIXIS, INC.
170 HARBOR WAY
P.O. BOX 511
SOUTH SAN FRANCISCO, CA 94083-0511

EXAMINER
MORAN, MARJORIE A

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 07/30/2003

7

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/846,758	LIU ET AL.	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears n the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *12-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 15-25* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Election/Restrictions

Applicant's election without traverse of Group I and a species of altered resistance to an herbicide, corresponding to claims 1-11 and 15-25, in Paper No. 6, filed 5/19/03 is acknowledged.

Claims 12-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 6.

An action on the merits of claims 1-11 and 15-25, as they read on the elected species of altered resistance to an herbicide, follows.

Information Disclosure Statement

The IDS filed 5/31/02 has been considered in full.

Priority

If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph; e.g. This application claims benefit of US Provisional Application 60/201,245, filed May 1, 2000.

Claim Objections

Claim6 is objected to because of the following informalities: the term "insertion" in line 1 should be --insertional--. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "essentially" in claim 20 is a relative term which renders the claim indefinite. The term "essentially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 9-10, 15 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over NEFF et al. (US 6,534,313, filed 3/16/00) in view of WAGNER et al. (US 2002/0157130, filed 3/9/2000).

Claim 1 recites a method of multigenerational plant analysis and data management comprising generating an mutation in the genome of a T0 plant with an insertional mutagen and collecting T1 seed from the mutated plant; growing T1 plants from the seed under selective conditions and assigning an ID number to each plant selected; analyzing the T1 plant and recording mutant traits in a database, wherein the database record is linked to the ID number; collecting T2 seed from the T1 plant and assigning an ID number to the T2 seed which is linked to the ID number of the T1 plant; growing T2 plants from the T2 seed; analyzing T2 mutant traits and recording them in the database those traits not observed in the T1 plant, wherein the records for T1 and T2 plants are associated. Claim 2 limits the insertional mutagen to an activation tagging vector. Claims 3-4 limit the activation tagging vector, specifically to a mirabilis mosaic

virus enhancer. Claim 5 limits the plant to Arabidopsis, tomato, or rice. Claim 6 limits the insertional mutagen to encode a selectable marker comprising antibiotic or herbicide resistance. Claim 9 limits the step of recording mutant traits to include obtaining a digital image of the plants and recording the image in the database. Claim 10 limits the mutant trait of claim 1 to be a morphological phenotype. Claim 15 limits the recording of mutant traits to recordation using predefined vocabulary. Claim 22 limits the method of claim 1 to identification of a dominant mutant trait by performing a hybrid cross by pollinating a wild-type plant with pollen from a T2 plant with a specific mutant trait, growing F1 plants from the hybrid cross, and identifying an F1 plant with the mutant trait. Claim 23 limits the method of claim 1 to identify a candidate gene responsible for a mutant trait by rescuing DNA flanking the insertional mutagen from a T1 or later generation plant, identifying a candidate gene from the rescued DNA, and identifying a candidate gene that is overexpressed in the transformed plant. Claim 24 limits the insertional mutagen of claim 23 to be an enhancer, the mutant trait to be dominant, and limits the method to further comprise preparing a heterologous gene construct comprising the enhancer, generating a transformed plant that is the same species as the T0 plant, generating and identifying transformed progeny that display the dominant mutant trait. Claim 25 limits the method of claim 24 to further comprise transforming a plant of a different species that the T0 plant, and generating and identifying transformed progeny that display the dominant mutant trait.

NEFF teaches a method of multigenerational plant analysis wherein Arabidopsis plants are transformed using enhancer elements from cauliflower mosaic virus, and

teaches that this mutation can be used to tag genes and identify dominant mutations (col. 3, lines 13-43 and col. 45, line 55-col. 46, line 7). NEFF teaches that the transgene can be inserted into the genome of a plant and teaches that seeds may be produced (col. 5, lines 24-31), and teaches that a nucleic acid construct for use in transformation may also include a selectable marker such as antibiotic resistance or herbicide resistance (col. 13, lines 20-35). NEFF specifically teaches that seeds from transformed plants may be collected to produce a second generation of plants which display a mutant phenotype (morphology) and that such plants may be self-crossed (col. 17, lines 42-46). NEFF teaches analysis of plants for mutant phenotypes (visual observation), and teaches analysis of T2 plants by digital imaging (col. 48, lines 55-59). NEFF teaches cross-pollination (col. 30, lines 23-28), teaches isolation (rescue) of tagged genes from T3 heterozygotes which result in a mutant phenotype by over-expression (col. 38, lines 12-34), and teaches transformation of plants from a different species (col. 41, lines 38-62 and col. 50, line 58-col. 52, line 3). NEFF does not teach recording his data in a database nor a mosaic mirabilis enhancer.

WAGNER teaches a method of mutigenerational plant analysis and associated data management similar to that of NEFF's wherein tomato seeds are transformed with an activation tagging vector, grown under selective conditions of herbicide or antibiotic resistance, and plants grown from the seeds are evaluated for mutations, specifically changes in morphological traits, wherein each plant and its progeny are assigned an identifier and linked to its associated mutant phenotype in a database (pp. 11-12 and Table 1). WAGNER teaches that an enhancer which may used in his insertional vector

is one derived from mirabilis mosaic virus (MMV), and teaches that this enhancer is similar in function to a CMV enhancer (p. 7, paragraphs 111 and 114).

It would have been obvious to one of ordinary skill in the art at the time of invention to have identified each transformed plant in the method of NEFF with a singular ID, and to have linked that ID to any mutant traits/phenotypes seen in subsequent progeny, as taught by WAGNER, where the motivation would have been to follow and perform further research on individual plant lines in order to rescue and identify gene(s) responsible for the mutant trait, as taught by WAGNER's method of doing so (pp. 12-13) and suggested by NEFF's cloning and molecular analysis of transformed plants (col. 45, line 55-col. 46, line 62). It would further have been obvious to have used an MMV enhancer as the enhancer element in the method of NEFF and WAGNER where the motivation would have been to use any enhancer element known in the art for use in transformation/activation tagging in plants, and where WAGNER teaches that an MMV enhancer is an art-recognized equivalent for the CMV enhancer of NEFF. No criticality or unexpected result has been shown for use of an MMV enhancer over a CMV enhancer in method of transformation/activation tagging of plants.

Claims 7, 11, and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over NEFF et al. (US 6,534,313, filed 3/16/00) in view of WAGNER et al. (US 2002/0157130, filed 3/9/2000) as applied to claims 1-6, 9-10, 15 and 22-25 above, and further in view of BHIDE et al. (US 6,150,158, filed 10/15/1998).

The claims recite a method of mutigenerational plant trait analysis and database management, as set forth above. Claim 7 limits the method to further comprise, before the step of assigning T1 ID numbers, the steps of transplanting transformed plants into wells of a multiwell plate wherein each perimeter well contains a plant and a central well contains a barcode; wherein the assigned ID numbers of the T1 plants derives from the barcode and relative position of the plants. Claim 11 limits the analysis of mutant traits to a directed screen for altered resistance to an herbicide. Claim 18 limits the method of claim 1 to further include steps of querying a database for a specific mutant trait previously recorded, obtaining T2 seed associated with the queried trait, performing a directed screen on the seeds or on plants grown from the obtained seed, entering the results of the screen into the database. Claim 19 limits the mutant trait of claim 18 to be a morphological phenotype.

NEFF and WAGNER make obvious a method of multigenerational plant trait analysis and associated database management, as set forth above. Both NEFF and WAGNER teach directed screening for altered resistance to plant pathogens of various types (see NEFF at col. 18 and WAGNER at paragraph 27), and WAGNER teaches querying a database for a particular mutant trait (see Example 2), but neither specifically teaches a directed screen for altered herbicide resistance. WAGNER teaches potting up and identifying individual plants (paragraph 204), but neither NEFF nor WAGNER teaches transplanting transformed plants into wells of a multiwell plate nor use of a barcode.

BHIDE teaches growing plants, specifically Aribidopsis, in individual wells of microtiter plates and teaches directed screens for herbicide resistance on plants grown in such plates (col. 25, line 6-col. 27, line 9). BHIDE further teaches that his plates may be identified with barcodes (col. 16, lines 26-32).

It would have been obvious to one of ordinary skill in the art at the time of invention to have transplanted the seedlings in the method of NEFF and WAGNER to individual wells of a multiwell plate, identified by barcode, in any pattern desired, as taught by BHIDE, where the motivation would have been to automate growth and analysis such that high-throughput screening of whole plants (e.g. resistance to an herbicide) may be accomplished with less space, labor, and test compound, as taught by BHIDE (abstract). It would further have been obvious to have screened for mutant traits related to altered resistance to an herbicide, as taught by BHIDE, in the method of NEFF and WAGNER where the motivation would have been to find mutants with altered resistance to a pathogen (i.e. plant toxin), as taught by both WAGNER and NEFF, wherein herbicides are known to be plant toxins, and where BHIDE teaches that knowledge of herbicidal resistance is known to be of interest in agricultural production (col. 1, lines 15-35). One skilled in the art would reasonably have expected success in growing the transplanted seedlings in the method of WAGNER and NEFF in the multiwell plates of BHIDE, and in performing directed screens for herbicide resistance on such seedlings, because BHIDE teaches that seedlings can be grown and screened in his plates.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over NEFF et al. (US 6,534,313, filed 3/16/00) in view of WAGNER et al. (US 2002/0157130, filed 3/9/2000) and BHIDE et al. (US 6,150,158, filed 10/15/1998) as applied to claims 1-7, 9-11, 15, 18-19 and 22-25 above, and further in view of WILLIAMES (AU 9516254).

The claims recite a method of mutigenerational plant trait analysis and database management, wherein plants are grown in a multiwell plate identified by a barcode, as set forth above. Claim 8 limits the recording of mutants traits of claim 7 to steps of using a hand-held electronic data entry device equipped with a barcode scanner.

NEFF, WAGNER, and BHIDE make obvious a method of mutigenerational plant trait analysis and database management, wherein plants are grown in a multiwell plate identified by a barcode, as set forth above. None of NEFF, WAGNER, or BHIDE specifically teach a hand-held barcode scanner.

WILLIAMES teaches monitoring growth of seedlings with a bar code system and use of a hand-held barcode scanner (abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to have used a hand-held barcode scanner, as taught by WILLIAMES, to monitor growth and other traits of seedlings in the method of NEFF, WAGNER, and BHIDE, where the motivation would have been to facilitate automation and seedling growth and handling, as taught by WILLIAMES, and where automation is taught to be desirable by BHIDE.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over NEFF et al. (US 6,534,313, filed 3/16/00) in view of WAGNER et al. (US 2002/0157130, filed 3/9/2000), BHIDE et al. (US 6,150,158, filed 10/15/1998), as applied to claims 1-7, 9-11, 15, 18-19 and 22-25 above, and further in view of USMANOV (Fiziologiya Rastenii (1999) vol. 46 (3), pp. 492-494).

The claims recite a method of mutigenerational plant trait analysis and database management, as set forth above. Claim 16 limits the collection of T2 seed to further comprise distribution of seed into a plurality of containers and storage under conditions that allow long-term recovery of seeds.

NEFF, WAGNER, and BHIDE make obvious a method of mutigenerational plant trait analysis and database management, wherein plants are grown in a multiwell plate identified by a barcode, as set forth above. NEFF teaches use of T2 and T3 seeds (col. 38, lines 21-24 and col. 45, lines 56-66), and therefore necessarily teaches collection of T2 seeds. None of NEFF, WAGNER or BHIDE teaches storage of seeds under conditions for long-term recovery and germination.

USMANOV teaches storage conditions for long-term recovery and germination of Arabidopsis seeds (abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to have processed seeds for long-term recovery, as taught by USMANOV, in the method of NEFF, WAGNER, and BHIDE, where the motivation would have been to maintain germination of seeds over a period of years, as taught by USMANOV.

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over NEFF et al. (US 6,534,313, filed 3/16/00) in view of WAGNER et al. (US 2002/0157130, filed 3/9/2000), BHIDE et al. (US 6,150,158, filed 10/15/1998), and USMANOV (Fiziologiya Rastenii (1999) vol. 46 (3), pp. 492-494) as applied to claims 1-7, 9-11, 15, 16, 18-19 and 22-25 above, and further in view of SANDVIK et al. (US 5,664,402)

The claims recite a method of mutigenerational plant trait analysis and database management, wherein plants are grown in a multiwell plate identified by a barcode, as set forth above. Claim 17 limits the storage containers of claim 16 to comprise a barcode including the T2 ID.

NEFF, WAGNER, BHIDE, and USMANOV make obvious a method of mutigenerational plant trait analysis and database management, wherein plants are grown in a multiwell plate identified by a barcode, and wherein seed is collected into multiple containers for long-term storage, as set forth above. None of NEFF, WAGNER, BHIDE, or USMANOV teaches barcoding seed storage containers.

SANDVIK teaches collection of seeds from plants wherein the seeds are distributed into multiple containers, identified by barcode (col. 5, lines 6-12), and processed for storage (abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to have stored seeds in containers identified by barcodes, as taught by SANDVIK, where the motivation would have been to identify the origin of the seeds in each container, as taught by SANDVIK.

Claims 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over NEFF et al. (US 6,534,313, filed 3/16/00) in view of WAGNER et al. (US 2002/0157130, filed 3/9/2000), BHIDE et al. (US 6,150,158, filed 10/15/1998), and USMANOV (Fiziologiya Rastenii (1999) vol. 46 (3), pp. 492-494) as applied to claims 1-7, 9-11, 15, 16, 18-19 and 22-25 above, and further in view of TERRYN et al. (IDS ref: FEBS Letters (1999) vol. 452, pp. 3-6).

The claims recite a method of mutigenerational plant trait analysis and database management, wherein seed from mutated plants is collected into multiple containers for long-term storage, as set forth above. Claim 20 limits the method of claim 16 to further comprise repeating all the steps of claim 1 such that "essentially" every gene in the genome of the plant being analyzed is mutated. Claim 21 limits the plant of claim 20 to Arabidopsis.

NEFF, WAGNER, BHIDE, and USMANOV make obvious a method of mutigenerational plant trait analysis and database management, wherein seed from mutated plants is collected into multiple containers for long-term storage, as set forth above. NEFF specifically teaches mutating Arabidopsis plants, and WAGNER teaches that a method of insertional mutagenesis may be used to mutate multiple genes (abstract). NEFF, WAGNER, BHIDE, and USMANOV do not specifically teach mutating "essentially" every gene in a plant genome.

TERRYN teaches that insertional mutagenesis can be used to randomly interrupt genes, and teaches that a mutant for every gene of the Arabidopsis genome should be known (p. 5).

It would have been obvious to one of ordinary skill in the art at the time of invention to have mutated "essentially" every gene in the Arabidopsis genome, as taught by TERRYN, using the method of NEFF, WAGNER, BHIDE, and USMANOV, where the motivation would have been to characterize the function and/or expression of every gene in a plant genome, as taught by TERRYN (pp. 1 and 5).

Conclusion

Claims 1-11 and 15-25 are rejected; claims 12-14 are withdrawn.

The prior art made of record and not relied upon which is considered pertinent to applicant's disclosure is JOHNSON et al. (US 6,455,758, filed 7/13/99), who teaches databases for use in plant breeding wherein phenotypic traits and genotypes are recorded and linked to each other (col. 4, lines 49-68). It is noted that JOHNSON specifically teaches that his databases may be used to link a genetic marker and phenotype in successive generations of plants, including hybrids (col. 6, lines 25-42).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703)

308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3524.

MARJORIE MORAN
PATENT EXAMINER

mam
July 28, 2003